

## Thinking time directive (Onslow's law)

Everyone seems to be talking about the new EU working time directive. This limits the number of hours a week we are allowed to work and will have a negative effect on healthcare services. No-one seems to have considered how those same healthcare services would benefit from a thinking time directive. *Bandolier*'s vision is for such a directive, to declare protected hours for people to be able to *think* about what they are or should be doing.

A little skilling goes a long way, even more today when the electronic tools available to us are so powerful. So if *Bandolier* has any theme this month, it is about how to think, and how to use information.

The first example is one on handwashing to reduce hospital acquired infection. Here the issue is not one of finding the information, but using it. We take an extremely good example, from Geneva, and explore how to use the information to model the likely impact in our hospital.

The second example is finding and using information about treatments for genital warts. A BMJ editorial recommends them, but without the bottom line. So it's a question of a bit of searching, a bit of reading, a bit of data extraction, a back of envelope calculation, and voilà, an NNT.

Then a wizzo new test is announced in the newspapers. So we show how it is possible to do some swift information retrieval and evaluation to work out whether or not it is important.

## Conference time

When space permits *Bandolier* likes to carry announcements about important conferences. Four this month, three in the paper version and one more on the net. In January is the PRICCE conference in Canterbury on NSF's for heart disease. The Centre for Evidence-Based Medicine in Oxford has its annual jamboree on how to practice EBM in April. If you like the idea of the Blue Ridge mountains in the Spring, go for "Information Mastery: An Evidence-Based Approach to Information Management" in Charlottesville, also in April. Details at [www.med.virginia.edu/ed-programs/cme/ebm](http://www.med.virginia.edu/ed-programs/cme/ebm)

Last, but not least, is ICECAP in Alicante in September. The International Collaboration of Evidence-based Critical Care, Anaesthesia and Pain, is in association with the Cochrane review group on pain, palliative and supportive care, and the IASP special interest group on systematic reviews.

## WASHING HANDS REDUCES HOSPITAL-ACQUIRED INFECTION

*Bandolier* 73 examined the importance of hospital acquired infection to health services. In England it costs £1 billion a year, kills 5000 patients, and consumes the resources of 27 400 bed hospitals. Effective handwashing can reduce that substantially (*Bandolier* 67), though there are few reports of effects over long periods. A long-term hospital wide study, demonstrating that an effectively implemented handwashing policy reduced hospital acquired infection by half and saving precious resources [1], is welcome.

### Study

The study was started in the mid-1990s in the University of Geneva Hospitals. Handwashing behaviour was monitored and the incidence of hospital acquired infection measured. After a baseline survey the interventions began in January 1995. At several times from 1994 on, trained staff observed health professionals at prespecified time periods throughout the hospital. An additional measure of efficacy was the amount of alcohol-based handrub solution dispensed by the pharmacy. Hospital acquired infection was measured as the annual prevalence identified by infection-control nurses using CDC standard definitions, and the number of new cases of MRSA infection.

### Interventions

The components of the interventions included:

- ◆ A multidisciplinary project team including senior managers and representatives from each medical and hospital service department.
- ◆ Senior hospital management gave the programme a hospital-wide priority and regularly participated themselves in regular meetings of the project team.

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*The views expressed in Bandolier are those of the authors, and are not necessarily those of the NHSE*

- ◆ Posters emphasising the importance of hand washing, particularly disinfecting. Posters, often with cartoons, featured the name of the ward that designed the poster so that authorship could be recognised around the hospital. Housekeeping staff changed posters weekly. Over 70 different posters were produced.
- ◆ Individual bottles of alcohol-based chlorhexidine solution were distributed, including specially designed flat containers so that individuals could easily carry their own supply.
- ◆ Funding to implement the programme and for an additional nurse for four months to start the programme off.
- ◆ A series of grand rounds in individual medical departments.
- ◆ Feedback from results of surveys and hospital infection through hospital newsletters.

## Results

The proportion of observed instances where necessary handwashing did indeed take place increased from 48% in 1994 to 66% by the end of 1997. Moreover, there was a change in behaviour, with hands being more often disinfected than just washed. This was demonstrated by a five-fold increase in the amount of alcohol-based handrub used over the period (Table 1). Hospital-acquired infection prevalence fell from 17% in 1994 to 10% in 1998 (Table 1), New cases of MRSA fell by half (Figure 1).

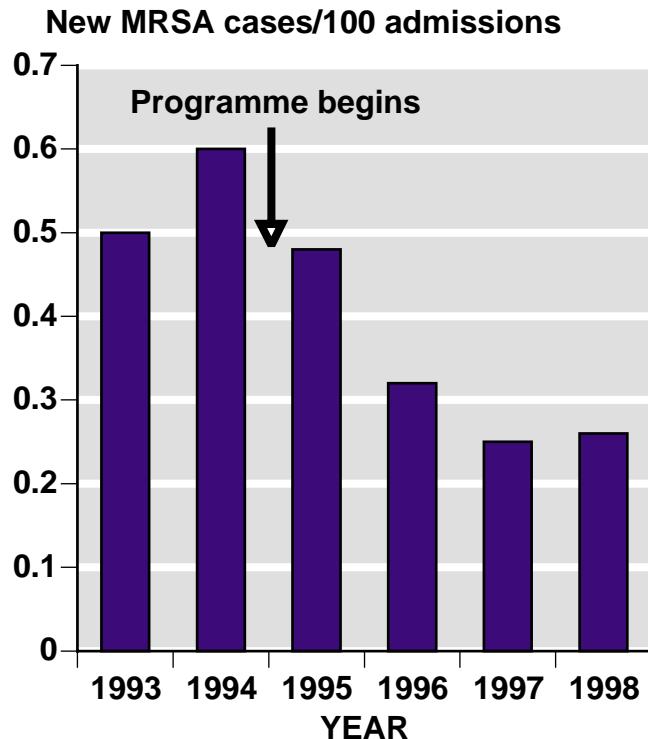
## Costs

The cost of the programme was estimated at no more than SFr 380,000 (£155,000; US\$270,000), including direct and indirect costs. The authors conservatively assumed that 25% of the observed reduction in infections was due to the hand washing programme, thereby preventing 900 infections. At an average cost estimate of about £1400 per infection, their estimate of overall savings of £1,260,000 far outweighed the costs.

## Comment

A UK report (*Bandolier* 73) estimated that a case of hospital acquired infection cost an extra £3150 and consumed an average of 14 extra bed-days. One of the main consequences

**Figure 1: New MRSA cases before and after the hand-washing programme started**



is bed blocking, and massive inefficiency in hospital systems. Reducing hospital acquired infection by half, exactly as seen in a UK example (*Bandolier* 67) would be equivalent to building, staffing and running 13 more 400 bed hospitals in England.

The characteristics of this study, apart from its typically Swiss thoroughness, are the same as examples in *Bandolier*'s sister publication, *ImpAct*. They are team work, ownership, audit, feedback, and a long-term commitment to improvement. That aside, there's nothing particularly clever being done. It really is easy, and it is done in most industries as a matter of course.

All hospital chief executives should read this paper several times. They should ask why their own institution is not already doing this. With this example, and in the full and certain knowledge that it saves resources, saves money, and is better for patients, there is no excuse not to follow the Swiss example. If they don't implement it the retirement cuckoo clock should be in the post.

**Table1: Use of hand disinfectant and hospital acquired infections**

Year	Alcohol-based handrub L/1000 patient days	New MRSA per 100 admissions	Hospital acquired infection (% patients)
1993	3.5	0.50	n/a
1994	4.1	0.60	16.9
1995	6.9	0.48	17.5
1996	9.5	0.32	14.5
1997	10.9	0.25	9.0
1998	15.4	0.26	9.9

## Unhealthy economics

And that is where this particular article ended, until, that is, we met a man upon the stairs. This particular man was one of life's cynics whose attitude was something like - "you never save anything in the NHS, so it's not worth bothering". Hang on a minute: that is unhealthy economics, so the argument needs extending to demonstrate the benefits in even starker detail.

We think the argument goes something like this. The hand-washing programme saved 900 infections. The average additional cost of a patient with hospital-acquired infection was £3154 and their average additional hospital stay was 14 days from a UK report (*Bandolier* 73). So 900 infections would consume £2.85 million, and 12,600 bed days more than if these patients did not have a hospital-acquired infection. Ninety of the 900 patients would die.

We could spend that wasted £2.85 million on a package that would include:

- 1 a hospital infection programme costing £155,000
- 2 care for an extra 1575 patients without hospital acquired infection using the 12,600 bed days saved at a cost of £2.56 million (1575 times £1628, or 8 days, from *Bandolier* 73 for average patients without infection)
- 3 £120,000 to spend in other ways (staff training or more initiatives to make the hospital better, perhaps)
- 4 fewer deaths in hospital.

Now this is all back-of-envelope stuff. But even in this simple examination the concept of hand-washing programmes can be seen as being no-brainers. This type of analysis should make the man on the stairs go away.

But no. The man on the stairs laughs uproariously, and tell us that we would never get the £155,000 new money because there is no budget for it. He thinks that budget-based medicine rules.

It shouldn't. It is possible to treat more patients better with the same resources. If it is possible, it should happen. We can measure the effectiveness of handwashing programmes through infection rates, deaths, and patient throughput. It isn't as if we want the £155,000 all at once. It is spread over several years in a big institution with a huge budget.

One of the benefits of a thinking time directive would be to generate time to think through the implications of doing the simple things right - an extension of doing the right things right, and at the right time. Handwashing is but one example of how to do more with less.

### References:

- 1 D Pittet et al. Effectiveness of a hospital-wide programme to improve compliance with hand hygiene. *Lancet* 2000 356: 1307-1312.

### THE APRIL 2001 OXFORD WORKSHOP ON HOW TO PRACTICE EVIDENCE-BASED MEDICINE

9-12 April 2001; Oxford, UK.

Chair: Dr Martin Dawes NHS R&D Centre for Evidence-Based Medicine; University of Oxford.

This workshop is designed to help clinicians and others to develop skills in evidence-based practice, with particular emphasis on formulating clinical questions, finding the evidence and critical appraisal. The workshop will be facilitated by tutors experienced in both the practice and teaching of EBM. More information and application forms may be obtained from:

Ms Bridget Burchell, NHS R&D Centre for Evidence-Based Medicine, University of Oxford, Nuffield Department of Clinical Medicine, Level 5, John Radcliffe Hospital, Headley Way, Headington, OXFORD OX3 9DU

Telephone: 01865 222941  
FAX: 01865 222901  
Email: admin@cebm.jr2.ox.ac.uk  
Internet: <http://cebm.jr2.ox.ac.uk/>

### IMPLEMENTATION OF SECONDARY PREVENTION OF CORONARY HEART DISEASE IN LINE WITH THE NSF

24 January 2001; Canterbury, UK.

Chair: Dr Tony Snell, East Kent Health Authority

This afternoon workshop is designed to help professionals to think through and implement best practice to fulfill the National Service Framework. Talks from John McMurray, Miles Fisher, Peter Livesey, Andrew Moore and John Heather will cover secondary prevention, diabetes, PRICCE, heart failure and waste in the NHS. More information and application forms may be obtained from:

Edwina Watt, Hayward Medical Communications, Rosemary House, Lanwades Park, Kentford, Near Newmarket, Suffolk CB8 7PW

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# GENITAL WART TREATMENTS

Anogenital warts (also called condylomas) are caused by the human papillomavirus (HPV). They occur predominantly in sexually active young adults, and have a variety of forms. They are common, with a million consultations annually in the USA, and over 50,000 newly diagnosed patients in the UK every year.

*Bandolier* was asked whether a recent editorial [1] suggesting that self-administered treatments were effective was correct. How can anyone tell? This seemed like a good excuse for a swift search for evidence as an exemplar of how a rapid review might be helpful and how it could be performed by a healthcare professional for, say, a health authority or primary care group wanting to make policy.

## Search

Two self-administered treatments were mentioned, imiquimod and podophyllotoxin creams. The way forward seemed to be to look for high quality and relevant trials. The ideal would be randomised double blind trials of self-administered treatment versus placebo in patients with properly diagnosed anogenital warts. Therefore the search used PubMed, the names of the treatments, and the sub-heading of randomised controlled trials. The Cochrane Library was also searched using a similar strategy. Searches revealed no previous systematic reviews.

For each treatment there was a page or two of possibly useful references (about 30-40). Most could be dismissed by reading the abstracts online. About 20 papers seemed relevant, and were ordered from the library.

## Outcomes

How does one choose an outcome in an unfamiliar area? A reasonable rule of thumb is to remember that while there can be many different outcomes, the highest hurdle for efficacy is patients cured (whatever that may be) and for harm is likely to be patients who discontinued because of adverse events. Patients with initial warts completely cleared at treatment end seemed a sensible efficacy outcome.

## Results

There were five relevant papers for imiquimod [2-6] and two for podophyllotoxin [7,8]. Each was randomised and double blind, had a placebo group, enrolled patients using a sensible diagnosis of genital warts (often with HPV confirmed), and had self-administered treatments. Several other papers were likely to be relevant, and for podophyllotoxin in particular there were a number of high quality studies with only active comparators.

Details of the trials are in Table 1 for imiquimod and Table 2 for podophyllotoxin. While all were randomised none gave details of randomisation, thus scoring one point out of two for randomisation. While all stated they were double blind, only two told us categorically that active and placebo treatments were identical, the others scoring one point

out of two [9]. Most discussed withdrawals.

## Imiquimod

Most studies used imiquimod 5% cream applied three times a week for 8-16 weeks. One [5] used a 2% cream applied twice daily for six weeks. One study [6] was specifically directed to patients with HIV infection, while the others omitted patients with HIV infection.

Results for the four studies on HIV-free patients [2-5] are shown in Figure 1 and Table 3. At the end of treatment with placebo, only 15/282 (5%) patients had their initial warts completely cleared. With imiquimod 146/284 (51%) of patients had warts completely cleared. The number needed to treat with imiquimod for six to 16 weeks to obtain one patient completely cleared who would not have been with placebo was 2.2 (95% CI 1.9 to 2.5).

The one study in HIV-infected patients [5] had only 7/65 (11%) patients cleared with active cream, compared with 2/35 (6%) with placebo.

Local cutaneous adverse events were common with imiquimod, notably erythema and skin irritation, with some burning and pain. Few patients discontinued therapy because of adverse events (Table 1).

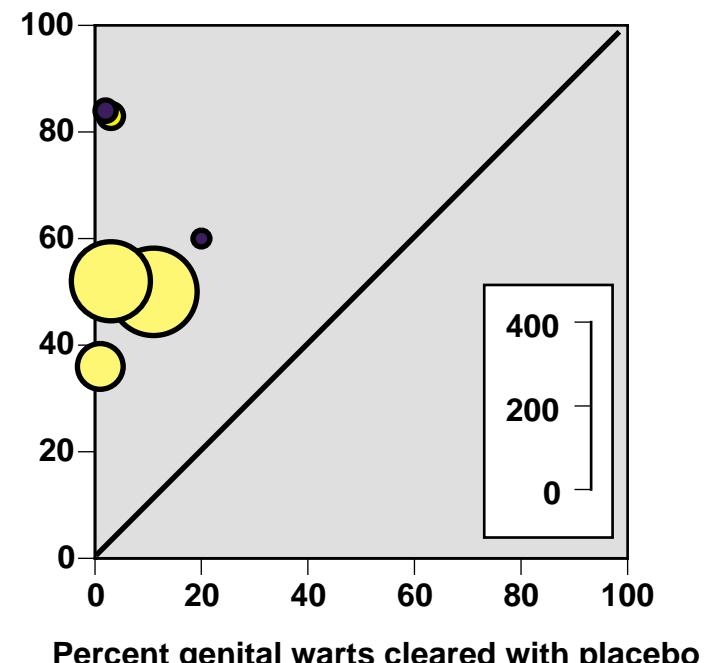
## Podophyllotoxin

Two studies examined 0.5% podophyllotoxin cream in women [7,8]. Application was twice daily for three consecutive days a week, for up to four weeks (Table 2).

Results are in Figure 1 and Table 3. At the end of treatment with placebo, only 4/40 (10%) patients had their initial warts completely cleared. With podophyllotoxin 37/50 (74%) of

**Figure 1: Imiquimod (open) and podophyllotoxin (filled) RCTs versus placebo**

**Percent genital warts cleared with treatment**



**Table 1: Randomised placebo-controlled trials of imiquimod cream for genital warts**

Reference, origin and quality score	Patients	Treatments	Design	Results	Adverse effects
Beutner et al, 1998a. USA R 1, DB 1, WD 1 Total 3/5	Men and women aged 18 or older with more than 2 and fewer than 50 external genital warts. HIV negative.	5% imiquimod cream 1% imiquimod cream placebo vehicle	Randomised, double blind, parallel group, with weekly and later two weekly visits for a maximum of 16 weeks, with further 12 week follow up.	Complete clearance 5% cream 49/94 1% cream 13/90 placebo 3/95	Local reactions included erythema, excoriation, flaking and erosion in all groups. Pain, burning and tenderness were more common with imiquimod than placebo. One patient in each imiquimod group discontinued because of skin reactions.
Beutner et al, 1998b. USA R 1, DB 2, WD 1 Total 4/5	Men and women aged 18 or older (90% men). HIV negative.	5% imiquimod cream placebo vehicle	Randomised, double blind, parallel group, with weekly visits for a maximum of 8 weeks, with further 10 week follow up.	Complete clearance 5% cream 18/51 placebo 0/57	Skin irritation greater with imiquimod than vehicle. Two patients withdrew because of this.
Edwards et al, 1998. USA & Canada R 1, DB 1, WD 1 Total 3/5	Men and women aged 18 or older with more than 2 and fewer than 50 external genital warts. HIV negative.	5% imiquimod cream 1% imiquimod cream placebo vehicle for 6-10 hours three times a week	Randomised, double blind, parallel group, with weekly and later two weekly visits for a maximum of 16 weeks, with further 12 week follow up.	Complete clearance 5% cream 54/109 1% cream 21/102 placebo 11/100	Local inflammation reactions were common, and more frequent with the 5% imiquimod cream. Two patients with the 5% cream were discontinued because of local reactions.
Syed et al, 1998. Pakistan R 1, DB 2, WD 1 Total 4/5	Women aged 18 to 45	2% imiquimod cream placebo vehicle Application twice a day for five consecutive days	Randomised, double blind, parallel group, with weekly and later two weekly visits for a maximum of 16 weeks, with further 16 week follow up.	Complete clearance 2% cream 25/30 placebo 1/30	Some mild adverse events, and no dropouts.
Gilson et al, 1999. UK & USA R 1, DB 1, WD 1 Total 3/5	Men and women aged 18 and older (mostly men) with HIV infection, and a minimum of 2 warts.	5% imiquimod cream placebo vehicle Applied for 6-10 hours three times a week.	Randomised, double blind, parallel group, with weekly and later two weekly visits for a maximum of 16 weeks, with further 16 week follow up.	Complete clearance 5% cream 7/65 placebo 2/35	One patient in each group discontinued because of local skin reaction. More local reactions with imiquimod than vehicle.

In all cases the outcome chosen was the proportion of patients with complete clearance of baseline warts. ITT analysis of all randomised patients. R is randomised, DB is double blind, WD is withdrawals and dropouts [9].

**Table 2: Randomised placebo-controlled trials of podophyllotoxin cream for genital warts**

Reference and origin	Patients	Treatments	Design	Results	Adverse effects
Syed et al, 1994: Pakistan $R = 1, DB = 1, WD = 0$ Total 2/5	Women aged 16 to 40 years.	0.5% podophyllotoxin cream 0.3% podophyllotoxin cream placebo vehicle Application twice daily for three consecutive days per week for up to four weeks	Randomised, double blind, parallel group, with weekly visits for a maximum of 4 weeks, with further 16 week follow up.	Complete clearance 0.5% cream 25/30 0.3% cream 16/30 placebo 0/20	Tenderness and burning sensation were reported local adverse reactions
Syed et al, 1995. Pakistan $R = 1, DB = 1, WD = 1$ Total 3/5	Women aged 18 to 40 years.	0.5% podophyllotoxin cream placebo vehicle Application twice daily for three consecutive days per week for up to four weeks	Randomised, double blind, parallel group, with weekly visits for a maximum of 4 weeks, with further 16 week follow up.	Complete clearance 0.5% cream 12/20 placebo 4/20	Not reported in detail

In all cases the outcome chosen was the proportion of patients with complete clearance of baseline warts. ITT analysis of all randomised patients. R is randomised, DB is double blind, WD is withdrawals and dropouts [9].

patients had warts completely cleared. The number needed to treat with podophyllotoxin for four weeks to obtain one patient completely cleared who would not have been with placebo was 1.6 (95% CI 1.3 to 2.1). Some local tenderness and burning was reported, but no patients discontinued because of this.

## Comment

The first thing is that an NNT of 2 is usually the marker of an effective treatment. For both treatments this was obtained using the high hurdle of patients completely cleared of the warts they had initially. Using lower hurdles, like at least 50% of the warts cleared, more impressive NNTs would be likely. The analysis was an intention-to-treat analysis, in which some patients lost to follow up were regarded as treatment failures.

There were local adverse events, but not so severe as to make many participants discontinue.

There are a few other things to think about though.

- ◆ First, especially for podophyllotoxin, there were several randomised trials with active comparators rather than placebo. Analysing these as well, though not as NNTs, would give more weight to the few patients in placebo-controlled trials.
- ◆ Second, there are more issues over efficacy. For instance, the analysis could have included analysis on warts appearing after treatment started. Then there is the issue of warts re-appearing after the end of treatment. And, of course, a detailed analysis of adverse events might be useful in telling prospective patients what to expect.
- ◆ Third is the issue of where these treatments are best used, in primary or secondary care? That may be more contentious, or easily incorporated into a treatment plan, according to local circumstances and budgets. An audit in Belfast [10] of 52 outpatients who had not benefited from a range of other treatments had similar outcomes to the randomised trials.

## DIY evidence

Where does the itch go when you scratch it? Just one of the many difficult questions. But is the process process of answering them one that can be done only by anoraks like *Bandolier*, or is it do-able elsewhere? Anyone with Internet access can search PubMed. Any UK doctor can join doctors.net and have access to the Cochrane Library online. Once the search is done, a local hospital library ought to be able to obtain the papers in a week or so.

To read, digest, and follow a few simple guidelines on systematic review and data presentation is not hard. So there really is no reason why any healthcare professional should not be able to do a swift analysis from time to time. But why don't we demand that companies have to present such independent reviews and analysis before they are allowed to market the drug?

**Table3: Imiquimod and podophyllotoxin NNTs**

Treatment	Number of trials	Active		Placebo		Relative benefit (95%CI)	NNT (95% CI)
		number/total	Percent (95%CI)	number/total	Percent (95%CI)		
Imiquimod	4	146/284	51 (46 to 57)	15/282	5 (3 to 8)	9.1 (5.6 to 15)	2.2 (1.9 to 2.5)
Podophyllotoxin	2	37/50	74 (62 to 86)	4/40	10 (1 to 19)	7.0 (2.7 to 18)	1.6 (1.3 to 2.1)

## References:

- 1 R Maw, G von Krogh. The management of anal warts. BMJ 2000 321: 910-911.  
 2 KR Beutner et al. Imiquimod, a patient-applied immune-response modifier for treatment of external genital warts. Antimicrobial Agents and Chemotherapy 1998 42: 789-794.  
 3 KR Beutner et al. Treatment of genital warts with an immune-response modifier (imiquimod). Journal of the American Academy of Dermatology 1998 38: 230-239.  
 4 L Edwards et al. Self-administered topical 5% imiquimod cream for external anogenital warts. Archives of Dermatology 1998 134: 25-30.  
 5 TA Syed et al. Management of female genital warts with an analog of imiquimod 2% in cream: a randomised, double-blind, placebo-controlled study. Journal of Dermatology 1998 25: 429-433.
- 6 RJ Gilson et al. A randomized, controlled, safety study using imiquimod for the topical treatment of anogenital warts in HIV-infected patients. AIDS 1999 13: 2397-2404.  
 7 TA Syed et al. Topical 0.3% and 0.5% podophyllotoxin cream for self-treatment of condylomata acuminata in women. Dermatology 1994 189: 142-145.  
 8 TA Syed et al. Management of genital warts in women with human leukocyte interferon-alpha vs. podophyllotoxin cream: a placebo-controlled, double-blind, comparative study. Journal of Molecular Medicine 1995 73: 255-258.  
 9 AR Jadad et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Controlled Clinical Trials 1996 17: 1-12.  
 10 JE Maitland, R Maw. An audit of patients who have received imiquimod cream 5% for the treatment of anogenital warts. International Journal of STD & AIDS 2000 11: 268-270.

## MELATONIN FOR JET LAG?

Many people are now used to intercontinental travel. For some, sometimes, travel either East or West can be accompanied by a horrible set of symptoms that include insomnia, fatigue, dullness of mind and a general feeling of awfulness. We call this jet lag, and attribute it, probably correctly, to rapid movement through many time zones. Our bodies and minds just don't know where they are.

Much time is taken up in pubs and at dinner parties discussing strategies to get over jet lag. Some consider alcohol a splendid remedy. Others different foods, like burgers and fries going West and salad and fasting going East. In recent years melatonin has been recommended in the press and elsewhere. *Bandolier* was asked for evidence that it worked. We found one excellent study [1] suggesting that it does not.

## Study

The study was randomised, double blind, double-dummy, and conducted on 339 Norwegian physicians who travelled to New York, spent at least five days there, and then returned home. On their return they had either melatonin 5 mg at bedtime on the day of travel, and then daily for five days, or 0.5 mg with the same schedule, or 0.5 mg taken progressively one hour earlier each day, or placebo.

## Outcome

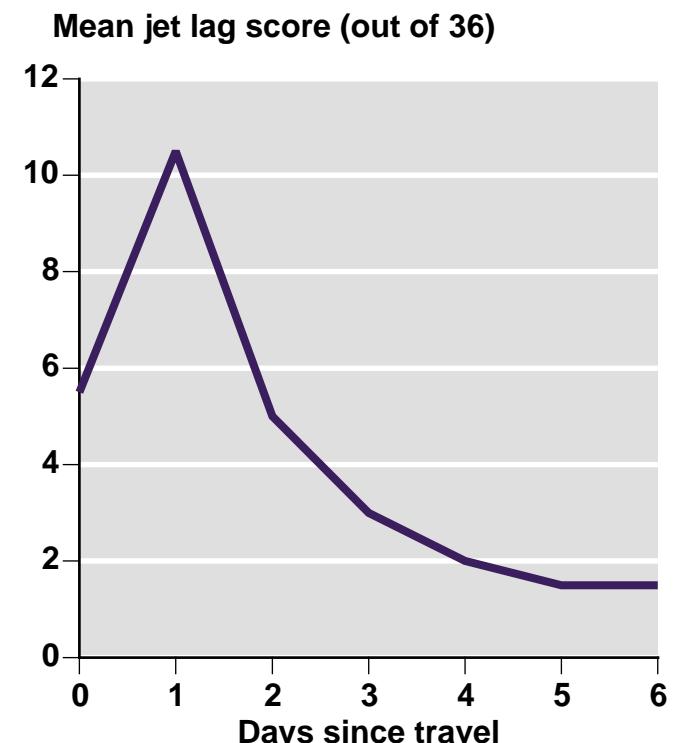
A jet lag score was devised and tested. It included nine items, comprising fatigue, daytime sleepiness, impaired concentration, decreased alertness, trouble with memory, physical clumsiness, weakness, lethargy, and light-headedness. Each was scored on a scale from 0 (no bother at all) to 4 (extremely bothered). The scale ranged from 0 to 36 points. Other outcomes were a patient global evaluation and some measures of sleep times.

## Results

On the last day in New York before returning to Oslo, the mean scores in the four groups were 4 to 6 out of 36. On the first day back in Oslo the means rose to 11 to 13 out of 36, and then fell on subsequent days to be about 1 out of 36 by the sixth day. Figure 1 shows only placebo as there was no difference overall between placebo or melatonin for jet lag score, nor any of its components, nor the global score. No sub group analysis showed any efficacy in any particular patient group.

One patient had difficulty in breathing and swallowing with melatonin low dose. These disappeared, but recurred on repeat challenge.

**Figure 1: Mean jet-lag scores for placebo treatment**



## Comment

On the results themselves, it is interesting how this fine large study contrasts with previous small studies with less adequate design which claimed benefit, even when it was not statistically significant. Unless there is some overwhelming reason to consider Norwegian physicians to be a peculiar bunch, different from the rest of humanity, melatonin won't work for us either.

The design of the study, and particularly the outcome measures, was meticulous, and would provide an exemplar for others wanting to research new or difficult areas. Particularly the jet lag score was designed after literature review, focus groups with frequent travellers, and by testing.

### References:

- 1 RL Spitzer et al. Jet lag: clinical features, validation of a new syndrome-specific scale, and a lack of response to melatonin in a randomized, double-blind trial. *American Journal of Psychiatry* 1999 156: 1392-1396.

## ICECAP CONFERENCE

The International Collaboration of Evidence-based Critical Care, Anaesthesia and Pain will be holding its first week-long workshop in Alicante in September 2001. The conference is in association with the Cochrane review group on pain, palliative and supportive care, and the IASP special interest group on systematic reviews.

The week-long conference is limited to those actively engaged on systematic reviews or method development. Participants will be expected to present data, and problems, and to participate in discussions about how to overcome them. Method development in evidence gathering and presentation, and clinical trial design, are the watchwords.

ICECAP is grateful to Merck & Co, Inc, for no-strings support that enables each public sector participant to have free accommodation in exchange for work. We hope to have travel bursaries available for certain categories. Participants from industry are encouraged, but will pay full rates.

Details in full on the *Bandolier* Internet site, or email Maureen ([maureen.woodford@pru.ox.ac.uk](mailto:maureen.woodford@pru.ox.ac.uk)) for information.

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## CANCER "HOLY GRAIL"?

Faced with a front page report on the *Daily Mail* of November 6<sup>th</sup> 2000 as well as an article in the previous day's *Observer* that a new cancer test was being called the "Holy Grail" on cancer testing, a few folks asked us for the evidence that backed this up. A brief tutorial, then, into finding and evaluating information like this.

## The test

The test is called DR-70, and purports to measure something called fibrinogen degradation product. This is thought to be formed in blood by the release of proteases from cancer cells. The test supposedly detects 13 different cancers from a single blood test that will cost £50, or \$100.

## Looking for information

The newspapers mentioned the *Journal of Immunoassay*. So we searched for DR-70 in this journal and found one peer reviewed paper from China [1]. No other papers were found on any search. On the Internet, we found an article about the test from the company that makes it [2]. We also downloaded and read the assay information booklet.

## What is the evidence?

If you have people who do not have cancer (as far as you know), and compare them with people who do have cancer (so far as you know), then those with cancer are more likely to have higher levels of what this test is measuring. This appears to be true for a variety of cancers. The Chinese study had 277 healthy subjects and 136 cancer patients with one of 13 different cancers. A number of abstracts from the early '90s had a small number of patients.

## Evaluating the evidence

*Bandolier* 70 described bias in diagnostic tests. The study design used to evaluate this test [1], of a group of patients already known to have the disease compared with a separate group of normal patients, was the most biased design. *Bandolier* 71 drew attention to evidence that 99% of 109 randomised trials from China had a positive result.

## Comment

The safest conclusion is that, at best, this is early days. There is no adequate information to demonstrate the value of this test, especially in people with illnesses other than cancer, and who already take medicines. Some people who do not have cancer will have a positive result. Some people who do have cancer will have a negative result. The trouble is that no one can tell you how many, or who.

### References:

- 1 D Wu et al. Clinical performance of the AMDL DR-70 immunoassay kit for cancer detection. *Journal of Immunoassay* 1998 19: 63-72.
- 2 [http://www.amdl.com/IVD\\_article/index.html](http://www.amdl.com/IVD_article/index.html)